REMARKS

Claims 1-28 are currently pending in the present application. Claims 1, 7, 8, 13, 15, 16, 21, 23, and 24 have been amended to clarify the claims language. In particular, independent claims 1, 13, and 21 have been amended to clarify that the substrate suspended in the medium is suitable for mycelia attachment. This limitation is supported, for example, at page 3, lines 17-22 or page 5, lines 26-30, of the specification. No new matter has been added by the above amendments.

Submitted herewith is a copy of a certified English language translation of Taiwanese Patent Application Serial No. 89103793, filed March 3, 2000, from which the present application claims priority. As the Examiner can see, the priority document is essentially identical in content to the present application. Accordingly, all pending claims are entitled to the March 3, 2000 priority date.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-28 have been rejected as indefinite for recitation of a number of terms that the Examiner has deemed to be impermissibly vague. Applicants submit that the above amendments have overcome each ground of rejection for indefiniteness. Nevertheless, if any issues regarding indefiniteness remain, the Examiner is encouraged to contact the undersigned so that those issues can be resolved quickly.

Rejection under 35 U.S.C. § 102(a)

Claims 1-4, 6-13, 15-21, and 23-28 are rejected as anticipated by Wu et al., Appl. Microbiol. Biotechnol. 53:542-544, May 2000. As noted above, all pending claims are entitled to the March 3, 2000 priority date of Taiwanese Patent Application Serial No. 89103793, before publication of Wu. Consequently, Wu is not prior art against the pending claims, and the rejection should be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claims 1-4, 13, and 21 are rejected as anticipated by Yamaguchi et al. (U.S. Patent No. 3,765,906). Applicants traverse this rejection on the ground that Yamaguchi does not describe fermenting filamentous fungi in a bioreactor using a nutritional substrate (e.g., a grain substrate) suitable for mycelia attachment. As described at page 3, lines 17-22, of the specification, an advantage of the invention is a nutritional substrate (e.g., grain particles) that

allows mycelia attachment, which decreases destruction of the fungi in a bioreactor, thereby increasing yields from the culture. Yamaguchi neither describes nor suggests using a nutritional substrate suitable for mycelia attachment in a bioreactor, as is required in independent claims 1, 13, and 21.

Instead, Yamaguchi prefers to include common substituents (e.g., carbon sources) that do not allow for mycelia attachment. These substituents include rice powder (Example 1), yeast extract (Example 3), defatted soybean meal (Example 6), peptone (Example 7), casein (Example 8), or mixtures of polypeptides (Example 10). None of the substituents included in Yamaguchi's media allows for mycelia attachment in a bioreactor. Accordingly, Yamaguchi does not anticipate independent claims 1, 13, or 21. In addition, because dependent claims 2-4 depend from claim 1, these claims too are distinguishable from Yamaguchi.

Rejections under 35 U.S.C. § 103(a)

Claims 6, 11, 12, 19, 20, 27, and 28 are rejected as obvious over Yamaguchi in view of Johal et al. (U.S. Patent No. 4,954,440) and Eyal et al. (U.S. patent No. 5,077,201). Each of the rejected claims directly or indirectly depend from claim 1, 13, or 21. Yamaguchi and its deficiencies are discussed above. Neither Johal nor Eyal alleviate those deficiencies, e.g., neither of the secondary references describe or suggest using a nutritional substrate that allows for mycelia attachment in a bioreactor. At best, Johal describes a synthetic matrix, such as polyurethane, for passive adsorption, but certainly not a nutritional substrate (e.g., col. 5, lines 51-52. Accordingly, the rejected claims are nonobvious over the cited references.

Claims 5, 7-8, 14-16, and 22-24 are rejected as obvious over Yamaguchi in view of Yueh et al. (U.S. Patent No. 4,418,080) and Haas et al. (U.S. Patent No. 4,031,250). Each of the rejected claims directly or indirectly depend from claim 1, 13, or 21. Yamaguchi and its deficiencies are discussed above. Neither Yueh nor Haas alleviate those deficiencies. In fact Yueh and Haas do not describe bioreactor fermentation at all and therefore are silent on what constituents should or should not be used in a bioreactor. As discussed, one basis for the claimed invention was a realization that bioreactor yields can be increased by employing a nutritional substrate that allows for mycelia attachment. Yueh and Haas, as well as Yamaguchi, do not recognize this advantage. Consequently, the Examiner has failed to provide a motivation in the

cited references necessary to combine the references to achieve the claimed methods, and therefore the rejected claims are patentable over the cited references.

Claims 9, 10, 17, 18, 25, and 26 are rejected as obvious over Yamaguchi in view of Yueh and Haas, and further in view of Tung et al. (Bioprocess Engineering 17:1-5, 1997). Each of the rejected claims directly or indirectly depend from claim 1, 13, or 21. Yamaguchi, Yueh, Hass, and their deficiencies have been discussed above. Tung has been cited for its description of an air-lift bioreactor. However, Tung does not suggest or describe the use of a nutritional substrate that allows for mycelia attachment in Tung's bioreactor, in part because Tung (or any other cited reference for that matter) fails to recognize the advantage of doing so. Thus, there is no motivation to combine the references to achieved the claimed methods.

Even if the Examiner should find motivation to combine two or more of the cited references to obtain a method falling within independent claims 1, 13, or 21, which applicants do not concede, that prima facie case of obviousness is rebutted by the unexpectedly superior yields provided by the invention.

Applicants ask that all claims be allowed. Enclosed is a $55 check for the Petition for Extension of Time fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 4-6-01

John T. Li
Reg. No. 44,210

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

1. (Amended) A method for cultivation of filamentous fungi comprising the steps of:

(a) preparing a medium comprising a suspended nutritionally solid substrate suitable for mycelia attachment; and

(b) inoculating [an inoculum into] said medium [comprising said nutritionally solid substrate] with said filamentous fungi in a bioreactor to carry out fermentation.

7. (Amended) The method as claimed in claim 1, [further comprising a step of inoculating] wherein step (b) comprises culturing said filamentous fungi [after step (a) to obtain said inoculum, and then inoculating said inoculum into said medium comprising said nutritionally solid substrate in a bioreactor to carry out fermentation] prior to introduction into said medium.

8. (Amended) The method as claimed in claim 7, wherein [the step of inoculating said filamentous fungi] step (b) comprises:

(1) inoculating said filamentous fungi from a stock culture to a new agar plate and incubating in an incubator for [5 ~ 7] about 5 to 7 days;

(2) washing spores and mycelia of the filamentous fungi grown on said plate with sterile water;

(3) cultivating said [spores/mycelia] spores and mycelia in a medium comprising a nutritionally solid substrate by shaking, to form a culture; and

(4) inoculating [a] the culture, after being cultivated for [36 ~ 48] about 36 to 48 hours, [at step (3)] into [a] the bioreactor.

13. (Amended) A method for cultivation of *Monascus* species by using a suspended grain substrate comprising the steps of:

(a) preparing a medium comprising a suspended grain substrate suitable for mycelia attachment; and

(b) inoculating [an inoculum into] said medium [comprising said grain substrate] with said *Monascus* species in a bioreactor to carry out fermentation.

15. (Amended) The method as claimed in claim 13, [further comprising a step of inoculating] wherein step (b) comprises culturing said *Monascus* species [after step (a) to obtain said inoculum, and then inoculating said inoculum into said medium comprising said nutritionally solid substrate in a bioreactor to carry out fermentation] prior to introduction into said medium.

16. (Amended) The method as claimed in claim 15, wherein [the step of inoculating said *Monascus* species] step (b) comprises:

(1) inoculating said *Monascus* species from a stock culture to a new agar plate and incubating in an incubator for [5 ~ 7] about 5 to 7 days;

(2) washing spores and mycelia of the filamentous fungi grown on said plate with sterile water;

(3) cultivating said [spores/mycelia] spores and mycelia in a medium comprising a grain substrate by shaking, to form a culture; and

(4) inoculating [a] the culture, after being cultivated for [36 ~ 48] about 36 to 48 hours, [at step (3)] into [a] the bioreactor.

21. (Amended) A method for producing metabolites from the cultivation of *Monascus* species by using a suspended grain substrate comprising the steps of:

(a) preparing a medium comprising a suspended grain substrate suitable for mycelia attachment; and

(b) inoculating [an inoculum into] said medium with said *Monascus* species [comprising said grain substrate] in a bioreactor to carry out fermentation.

23. (Amended) The method as claimed in claim 21, [further comprising a step of inoculating] wherein step (b) comprises culturing said *Monascus* species [after step (a) to obtain said inoculum, and then inoculating said inoculum into said medium comprising said

nutritionally solid substrate in a bioreactor to carry out fermentation] prior to introduction into said medium.

24. (Amended) The method as claimed in claim 23, wherein [the step of inoculating said *Monascus* species] step (b) comprises:

(1) inoculating said *Monascus* species from a stock culture to a new agar plate and incubating in an incubator for [5 ~ 7] about 5 to 7 days;

(2) washing spores and mycelia of the filamentous fungi grown on said plate with sterile water;

(3) cultivating said [spores/mycelia] spores and mycelia in a medium comprising a grain substrate by shaking, to form a culture; and

(4) inoculating [a] the culture, after being cultivated for [36 ~ 48] about 36 to 48 hours, [at step (3)] into [a] the bioreactor.